In the Specification

Please amend the specification as follows:

Please replace the title of the application with the following title:

Methods of Preventing Transplant Rejection Using Immunotoxins and Costimulation Blockade of CD154 and CD28

Please replace the paragraph on the first page of the specification prior to the background of the invention with the following paragraph:

-- The present application is a 35 U.S.C. § 371 national phase application from, and claims priority to, International Patent Application PCT/US00/00284, filed July 06, 2001 (published under PCT Article 21(2) in English), which claims ~~priority to~~ benefit of U.S. Provisional Patent Application Serial No. 60/115,252, filed January 08, 1999 ~~which applications are hereby incorporated herein in their entirety by reference~~.--

Please replace the paragraph between page 16, line 24 and page 17, line17 with the following paragraph.

-- The mutated toxins are produced and purified analogously to the parent toxin except that low levels of reducing agent (equivalent to 2 mM betamercaptoethanol) are included in the purification to protect the unpaired introduced -SH group. Thioether chemical coupling is achieved to a single unpaired cysteine within the divalent antibody construct at either residue 414 in domain γCH3 or residue 575 in domain μCH4 when this domain is included. In this case domain γCH3 is mutated C414A to provide only a single coupling site. An advantage of including μCH4 is enhanced stability of the divalent antibody. A disadvantage is that the extra domain increases size and thereby reduces the secretion efficiency during antibody production.

The advantage of terminating with the γCH3 domain is that, in another variant, a His6 purification tag can be added at either the μCH2 COOH or γCH3 COOH terminus to facilitate antibody purification. Another variant is to use the γ hinge region to form the interchain disulfide and to couple through a γCH3 or μCH4. This variant has the advantage of being smaller in size and places the toxin moiety closer to the CD3 epitope binding domains, which could increase toxin membrane translocation efficiency. A His tag can be included at the carboxy terminus as a purification aid. SH-CRM9 is concentrated to 10 mg/ml in PBS pH 8.5 and reacted with a 15 fold molar excess of bismaleimidohexane (BMH) (Pierce, Rockford, IL). Excess BMH is removed by passing over a small G25F column (Pharmacia, Piscataway, NJ). The maleimide derived toxin at about 5 mg/ml is now added to scUCHT1 divalent antibody at 10 mg/ml at room temperature. After 1 hr the conjugate is separated from non-reactive starting products by size exclusion HPLC on a 2 inch by 10 inch MODcol column packed with ~~Zorbax~~ ZORBAX® (DuPont) GF250 6 micron resin (for large scale production). Derivatives of ETA60EF61cys161 are also coupled to scUCHT1 divalent antibody by the same method. --

Please replace the paragraph between page 23, line 29 and page 24, line 4 with the following paragraph:

-- *MLR.* PBMC is isolated on Ficoll®-Hypaque (Sigma) and washed three times in RPMI/10% FCS. PBMC is used either fresh or cyropreserved until the assay date. A monocyte-depleted responder population is obtained by passing cells over a ~~Sephedex~~ SEPHADEX® G-10 (Thomas et al. (1991)). 100μl stimulator cells and 100μl responder cells (each 05. x 106 cells /ml) are plate in 96 well round bottom culture plates. On days 3, 5 and 7, plates are harvested and counted after 16 hours labeling with 2.5 uCi/well 3H-thymidine. --

Please replace the paragraph on page 28, lines 17-26 with the following paragraph:

-- *Antibody-Complement-mediated Cytolysis (ACC) Assay.* ACC can be performed as previously described (Derry et al. (1982)). Target cells are 51Cr labeled donor and third party ConA blasts in RPMI/10% FCS. 10ml of target cells (1x 106/ml) are incubated with 20ml diluted serum in triplicate for 45 minutes in 96-well round bottom plates at room temperature.

Rabbit compliment, diluted 1:8, is then added to each well (20 ml). Plates are incubated for 45 minutes at 37°C. After 100ml of cold media are added to each well, the plates are harvested and the supernatant is harvest on Skatron filters (Skatron, Sterling VA). Controls include spontaneous lysis (no compliment added) and maximum lysis (2% ~~TritonX-100~~ TRITON®-X100). Percent specific 51Cr release is then calculated. --